The Danish Stem Cell Center (DanStem) was established in late 2011 at the Faculty of Health Sciences, University of Copenhagen. Its mission is to establish internationally competitive stem cell research at the highest level with in Denmark and to establish new mechanisms to translate findings from this work into the clinic. It also seeks to promote stem cell biology within the Copenhagen area through organizing courses, international conferences, and hosting a regular seminar series that brings world leaders to speak in Copenhagen.

**RESEARCH AT DANSTEM**

DanStem has both virtual and physical entities. It is a virtual grouping of 9 stem cell groups in the Copenhagen area with a shared goal of developing new common research themes. Six of these groups are located in a central DanStem facility. The physical entity that is DanStem was established at the Panum Institute, and contains state of the art embryonic and induced pluripotent stem cell culture facilities, embryo culture and microinjection, flow cytometry, transcriptomics and imaging. In addition to the groups located in the facility, DanStem also contains groups elsewhere in Panum and in the Biotech Research and Innovation Centre (BRIC). All DanStem groups are invited to use these facilities and DanStem also provides a home and access to ESC culture to the revamped Transgenic Core at the university of Copenhagen. DanStem has invited other Danish groups to work with them and exploit these facilities through a program of competitive grant awards under the banner of ‘national collaboration’.

**DANSTEM COMPRISSES TWO SECTIONS**

DanStem is composed of two sections; a section for basic research in development and stem cell biology (BasicStem) supported by a 10-year grant from the Novo Nordisk Foundation and a section for translational research (TransStem) originally supported by a grant from the now abandoned Danish Council for Strategic Research. BasicStem explores fundamental mechanisms governing the ontogeny, renewal and differentiation of stem and/or progenitors cells in both development and in adult homeostasis. We also study how these processes become disturbed in disease states and TransStem facilitates the translation of such findings into clinical practice and commercialization.

Under the directorship of Prof. Henrik Semb, DanStem was established by coupling a series of international recruitments with internationally recognized research groups located at the University of Copenhagen. All DanStem groups are expected to work at the highest level internationally and bring their strong network of collaborations to Copenhagen. Presently, the Center consists of a total of 126 employees and has additional groups affiliated through a series of national collaboration grants. The nine core groups, led by Josh Brickman, Elisabetta Ferretti, Anne Grapin-Botton, Kristian Helin, Elke Ober, Ole William Petersen, Bo Porse, Henrik Semb, and Palle Serup, all address basic questions in stem cell and developmental biology with the overall aim of developing new therapeutic approaches for diabetes, liver disease, and cancer.
RESEARCH GROUPS

Stem Cells and Developmental Biology
The Brickman lab’s main interest is in the mechanisms by which transcription regulates cellular potency and commitment. How do cells select specific fates? Can they transcriptionally sample different ones and does this explain phenomena like stem cell toti- or pluripotency? What mechanisms result in the irreversible activation of differentiation programs? To approach these questions, they use ES cells, pre and post implantation embryos and Xenopus as models.

The Ferretti lab is interested in the targets of TALE class of homeodomain proteins and how this may explain cell type specific responses to signalling in early embryonic differentiation, organogenesis and tissue homeostasis. The lab also aims to understand how defects in the TALE networks affect early steps of cancer metastasis such as the gain of invasive and migratory properties by tumour cells.

The Grapin-Botton lab focuses on cell and tissue architecture and how this combines with signalling to control cell differentiation and fate choice. They use mouse genetics and have developed 3D in vitro culture systems that simplifies pancreas development and analysis. Their work provides insight into human syndromes of impaired pancreas development.

The Ober lab uses zebrafish as a model to study mechanisms that control the specification of liver progenitors from the foregut endoderm. Their work is focused on signalling in liver development and how molecular mechanisms regulating development may compare with mechanisms controlling regeneration.

The Semb lab’s main goals are to understand how cell polarity and tissue architecture control cell fate specification, and to translate this knowledge into efficient and reliable strategies for regenerative medicine in diabetes. They use a combination of mouse models and human pluripotent stem cells to investigate these goals, and as tools to understand pancreatic disease.

The Serup lab is interested in understanding how intercellular signalling controls cell fate choice during development. They develop new reporters to study signalling events in mouse embryos as well as mouse and human ES cell cultures, and to perform screens for novel genes controlling target gene activity. Their main focus is on how Notch signalling regulates pancreatic development.

Cancer Stem Cells
The Helin lab explores mechanisms that control cell-fate decisions in stem cells, differentiated cells, and tumour cells. They use genomic and proteomic approaches to identify and characterize genes and mechanisms involved in cancer development as well as more targeted methods to understand the function of cancer relevant gene families with a focus on epigenetic regulators.

The Petersen lab focuses primarily on understanding the morphogenesis and differentiation of normal and neoplastic human breast tissue. To this end they establish cell lines from both non-malignant and malignant breast tissue and use these to ask questions about the growth factor control of differentiation and lineage associations in normal breast epithelial cells and cancer cells.

The Porse lab’s main research area is the provision of a better understanding of the role of transcription factors in normal and malignant hematopoiesis. They identify novel oncogenes that collaborate with a mutant form of the tumour suppressor C/EBP in leukemogenesis and characterize the oncogenic properties of these. A second area is to characterize the importance of nonsense-mediated mRNA decay in vivo.

INTERNATIONAL AND SYNERGETIC RESEARCH ENVIRONMENT
One common theme that linked the international recruitment drive at DanStem has been developing an internationally visible critical mass of stem cell research focused in a specific area. As a large number of the initial recruits to DanStem have been interested in stem and progenitor cells associated with the visceral organs, or the endoderm germ layer, DanStem has rapidly established itself as a leading centre in Europe in this area.

This was recognized in DanStem leading of an EU 7th Framework Programme Project ‘HumEn’ that includes four groups at DanStem (Brickman,
Grapin-Botton, Semb, and Serup) and is lead by Henrik Semb. The HumEn project brings together six leading European stem cell-research groups and three industrial partners in a coordinated and collaborative effort aimed at using different approaches to expand stem and progenitor cells to develop glucose-responsive, insulin-producing beta cells for future cell-replacement therapy in diabetes. DanStem researchers also coordinate a Human Frontiers in Science Program that includes groups in Israel and USA.

DanStem is also carving a unique ‘niche’ for itself in the area of multi-disciplinary interaction. Three DanStem groups recently joined together with three groups at the Niels Bohr Institute to build a Centre of Excellence with the support of The Danish National Research Foundation, Grundforskningsfonden, Stem Cell Decision Making Center, (StemPhys). The center will exploit the unique opportunity that stem cell systems provide to deconstruct cell fate choice, explore the physical basis for decisions, and generate new quantitative and predictive models that can be used to understand differentiation. The long-term goal is to be able to manipulate the identity of cells through precise understanding of their behavior.

DISSEMINATION AND OUTREACH

DanStem researchers are actively involved in research-based training of undergraduates, PhD students and post-docs. Several internationally high profile PhD courses have been organized and the Center seeks to bring world leaders to Copenhagen to aid in the education of the next generation of stem cell biologists and clinicians. As eluded to in the beginning of this piece, DanStem hosts a seminar series where prominent national and international speakers present their results and latest state-of-the-art approaches relevant for the research areas within DanStem. These seminars are held at noon on Wednesdays roughly every second week and are open for all interested parties. A list of past and future speakers can be found at the DanStem website.

DanStem and the Novo Nordisk Foundation also organize a biannual conference entitled ‘The Stem Cell Niche’ that is part of the larger ‘Copenhagen Bioscience Conference’ series. These conferences provide a relaxed but intense opportunity for scientific interaction and provide funding for all accepted applicants to attend. Approximately 200 attendees (including speakers) are selected from the applicants to represent a range of participants from Denmark, Europe and the rest of the world.

DanStem is also interested in promoting stem cell research to the broader public. We actively engage the media, are happy to do educational programs in schools and have been involved in various Science Festivals such as the “Science in the City” festival held at ‘Carlsberg Byen’ as part of the ‘Into the body’ exhibition organized by the Faculty for Health Sciences (Figure 1).